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FILE COVERS 1907 - 13 Mar 2004 VOL 140 ISS 12

FILE LAST UPDATED: 12 Mar 2004 (20040312/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s (pompe or (glycogen (w) storage (w) disease))

248 POMPE

15 POMPES

250 POMPE

(POMPE OR POMPES)

47955 GLYCOGEN

350 GLYCOGENS

48000 GLYCOGEN

(GLYCOGEN OR GLYCOGENS)

314500 STORAGE

577 STORAGES

314722 STORAGE

(STORAGE OR STORAGES)

666587 DISEASE

186429 DISEASES

754838 DISEASE

(DISEASE OR DISEASES)

862 GLYCOGEN (W) STORAGE (W) DISEASE

L1 1017 (POMPE OR (GLYCOGEN (W) STORAGE (W) DISEASE))

=> s l1 and (tandem (w) mass (w) spectrometry)

38585 TANDEM

158 TANDEMS

38643 TANDEM

(TANDEM OR TANDEMS)

798409 MASS

71780 MASSES

836277 MASS

(MASS OR MASSES)

307314 SPECTROMETRY

560 SPECTROMETRIES

2  
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NEWS	4	DEC 08	INPADOC: Legal Status data reloaded
NEWS	5	SEP 29	DISSABS now available on STN
NEWS	6	OCT 10	PCTFULL: Two new display fields added
NEWS	7	OCT 21	BIOSIS file reloaded and enhanced
NEWS	8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS	9	NOV 24	MSDS-CCOHS file reloaded
NEWS	10	DEC 08	CABA reloaded with left truncation
NEWS	11	DEC 08	IMS file names changed
NEWS	12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS	13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAPplus
NEWS	14	DEC 17	DGENE: Two new display fields added
NEWS	15	DEC 18	BIOTECHNO no longer updated
NEWS	16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS	17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS	18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS	19	DEC 22	ABI-INFORM now available on STN
NEWS	20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAPplus
NEWS	22	FEB 05	German (DE) application and patent publication number format changes
NEWS	23	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS	24	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	25	MAR 03	FRANCEPAT now available on STN
NEWS EXPRESS	MARCH 5 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004		
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## 307632 SPECTROMETRY

(SPECTROMETRY OR SPECTROMETRIES)

7976 TANDEM (W) MASS (W) SPECTROMETRY

L2 6 L1 AND (TANDEM (W) MASS (W) SPECTROMETRY)

=&gt; d 12 1-6 kwic

L2 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

TI Analysis of a glucose tetrasaccharide elevated in **Pompe** disease  
by stable isotope dilution-electrospray ionization **tandem**  
**mass spectrometry**

AB Patients with **glycogen storage disease** type  
II (GSD II) typically excrete increased amts. of a glycogen-derived  
glucose tetrasaccharide, Glc $\alpha$ 1-6Glc $\alpha$ 1-4Glc $\alpha$ 1-4Glc  
(Glc4), in the urine. With the . . . of treatment. Glc4 is a good  
candidate biomarker for GSD II. A simple and robust method using stable  
isotope dilution-electrospray ionization-**tandem mass**  
**spectrometry** for the anal. of Glc4 in biol. samples was developed.  
A 13C6-labeled stable isotope internal standard was synthesized by  
transglycosylation. . .

ST glucose tetrasaccharide mass spectrometry **glycogen**  
**storage disease** urine

IT Blood analysis

Blood plasma

HPLC

Human

Isotope dilution mass spectrometry

Quality control

Urine analysis

(anal. of a glucose tetrasaccharide elevated in **Pompe** disease  
by stable isotope dilution-electrospray ionization **tandem**  
**mass spectrometry**)

IT **Tandem mass spectrometry**

(electrospray-ionization; anal. of a glucose tetrasaccharide elevated  
in **Pompe** disease by stable isotope dilution-electrospray  
ionization **tandem mass spectrometry**)

IT Electrospray ionization mass spectrometry

(tandem; anal. of a glucose tetrasaccharide elevated in **Pompe**  
disease by stable isotope dilution-electrospray ionization **tandem**  
**mass spectrometry**)

IT **Glycogen storage disease**

(type II; anal. of a glucose tetrasaccharide elevated in **Pompe**  
disease by stable isotope dilution-electrospray ionization **tandem**  
**mass spectrometry**)

IT 35175-16-7

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL  
(Biological study); USES (Uses)

(anal. of a glucose tetrasaccharide elevated in **Pompe** disease  
by stable isotope dilution-electrospray ionization **tandem**  
**mass spectrometry**)

L2 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

TI Determination of oligosaccharides in **pompe** disease by  
electrospray ionization **tandem mass**  
**spectrometry**

AB . . . need for biochem. markers to monitor the efficacy of therapy and  
methods to quantify these markers in biol. samples. In **Pompe**  
disease, the concentration of a tetrasaccharide, consisting of four glucose  
residues, is reputedly increased in urine and plasma, but faster. . .  
oligosaccharides, from biol. fluids. Methods: We optimized the  
derivatization of storage oligosaccharides with 1-phenyl-3-methyl-5-  
pyrazolone for the measurement, by electrospray ionization **tandem**  
**mass spectrometry**, of oligosaccharide concns. in urine  
(n = 6), plasma (n = 11), and dried-blood spots (n = 17) from  
**Pompe**-affected individuals. Age-matched control samples of urine

(n = 10), plasma (n = 28), and blood spots (n = 369) were. . . . mean tetrasaccharide concentration was increased in urine from infantile-onset (0.69-12 mmol/ mol. of creatinine) and adult-onset (0.22-3.0 mmol/mol of creatinine) **Pompe** individuals compared with age-matched controls. In plasma samples, an increased tetrasaccharide concentration was observed in some infantile patients (up to. . . . determine oligosaccharide concns. in a single 3-mm blood spot, but no differences were observed between blood spots from control and **Pompe**-affected individuals. Conclusions: Measurements of oligosaccharide concns. in urine by this new method have potential application for the diagnosis and monitoring of patients with **Pompe** disease. Plasma anal. may have limited application for infantile patients, but anal. of blood spots does not discriminate between controls. . . .

ST oligosaccharide **pompe** disease electrospray ionization  
tandem mass spectrometry

IT Blood analysis  
Blood plasma  
Body fluid  
Diagnosis  
Human

Tandem mass spectrometry

Urine analysis

(oligosaccharides determination in **pompe** disease by electrospray ionization tandem mass spectrometry)

IT Oligosaccharides, analysis

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(oligosaccharides determination in **pompe** disease by electrospray ionization tandem mass spectrometry)

IT **Glycogen storage disease**

(type II; oligosaccharides determination in **pompe** disease by electrospray ionization tandem mass spectrometry)

IT 89-25-8, 1-Phenyl-3-methyl-5-pyrazolone

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(oligosaccharides determination in **pompe** disease by electrospray ionization tandem mass spectrometry)

L2 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

TI Diagnostic methods for **Pompe** disease and other **glycogen storage diseases**

AB The invention concerns methods of screening subjects for lysosomal storage diseases, preferably **glycogen storage diseases**, using a tetrasaccharide as a biomarker. In a more preferred embodiment, subjects are screened for **Pompe** disease (i.e., **glycogen storage disease** type II). Also provided are neonatal screening assays. The present invention further provides methods of monitoring the clin. condition and efficacy of therapeutic treatment in affected subjects. Further provided are methods of measuring a tetrasaccharide biomarker by **tandem mass spectrometry**, preferably, as part of a neonatal screening assay for **Pompe** disease.

ST glycogen storage **Pompe** disease diagnosis tetrasaccharide HPLC mass spectrometry

IT Amniotic fluid  
Animal tissue  
Biomarkers (biological responses)  
Blood analysis  
Blood plasma  
Blood serum  
Body fluid  
Cell

Electrospray ionization mass spectrometry  
Glycogen storage disease

HPLC  
Human  
Immunoassay  
Liquid chromatography  
Lysosomal storage disease  
Mass spectrometry  
Newborn  
Purification  
Sputum

**Tandem mass spectrometry**

Urine analysis  
(diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT Blood analysis  
(dried blood spot; diagnostic methods for **Pompe** disease and  
other **glycogen storage diseases**)

IT Standard substances, analytical  
(internal; diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT Ecology  
(population; diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT **Glycogen storage disease**  
(type II; diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT **Glycogen storage disease**  
(type III; diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT **Glycogen storage disease**  
(type VI; diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT 35175-16-7 379261-84-4  
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL  
(Biological study); USES (Uses)  
(diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT 89-25-8, 1-Phenyl-3-methyl-5-pyrazolone 93-97-0, Benzoic anhydride  
94-25-7, Butyl p-aminobenzoate 27918-14-5, 2-Aminoacridone  
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
(diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

IT 34620-76-3, Maltopentaose 34620-77-4, Maltohexaose 379261-83-3  
RL: ARU (Analytical role, unclassified); ANST (Analytical study)  
(diagnostic methods for **Pompe** disease and other  
**glycogen storage diseases**)

L2 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

IT Electrospray ionization mass spectrometry  
Mass spectrometry

**Tandem mass spectrometry**

Time-of-flight mass spectrometry

(peptide mass determination by; peptide based DNA sequence identification

and

anal. and application to detection of polymorphism, mutations, and  
disease diagnosis)

IT **Glycogen storage disease**  
(type II; peptide based DNA sequence identification and anal. and  
application to detection of polymorphism, mutations, and disease  
diagnosis)

L2 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

TI Liquid chromatographic assay for a glucose tetrasaccharide, a putative  
biomarker for the diagnosis of **pompe** disease

AB . . . tetraglucose, normally excreted in the urine, has previously been  
shown to be elevated in a number of pathol. conditions including

**Pompe disease (glycogen storage disease type II)**, which is caused by a deficiency of the lysosomal enzyme acid  $\alpha$ -glucosidase. Concns. of Glc4 in both urine. . . . 1-5, 6-10, 11-20, and >20 yr, both in normal individuals and in a cohort of 21 patients with enzymically confirmed **Pompe disease**. The Glc4 concentration decreased with age in both groups, but all the patients had elevated Glc4 levels compared with age-matched controls. Electrospray **tandem mass spectrometry** was employed to establish the homogeneity of the HPLC peak for Glc4 and to investigate the identity of other unusual. . . . urine. Our results demonstrate that this method is suitable for application in clin. labs. to help establish the diagnosis of **Pompe disease**. (c) 2000 Academic Press.

ST glucose tetrasaccharide detn HPLC **Pompe disease**  
IT HPLC  
Urine analysis  
(glucose tetrasaccharide detn by HPLC for diagnosis of **Pompe disease**)  
IT **Glycogen storage disease**  
(type II; glucose tetrasaccharide detn by HPLC for diagnosis of **Pompe disease**)  
IT 35175-16-7  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(tetraglucose; glucose tetrasaccharide detn by HPLC for diagnosis of **Pompe disease**)  
L2 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
IT Electrospray ionization mass spectrometry  
Mass spectrometry  
**Tandem mass spectrometry**  
(for peptide anal.; methods and materials for peptide-based DNA sequence determination and anal.)  
IT **Glycogen storage disease**  
(type II, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

=> d 12 1-6, iall

L2 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:311407 CAPLUS  
DOCUMENT NUMBER: 140:90078  
ENTRY DATE: Entered STN: 23 Apr 2003  
TITLE: Analysis of a glucose tetrasaccharide elevated in **Pompe disease** by stable isotope dilution-electrospray ionization **tandem mass spectrometry**  
AUTHOR(S): Young, Sarah P.; Stevens, Robert D.; An, Yan; Chen, Yuan-Tsong; Millington, David S.  
CORPORATE SOURCE: Department of Pediatrics, Division of Medical Genetics, Biochemical Genetics Laboratory, Duke University Medical Center, Research Triangle Park, NC, 27709, USA  
SOURCE: Analytical Biochemistry (2003), 316(2), 175-180  
CODEN: ANBCA2; ISSN: 0003-2697  
PUBLISHER: Elsevier Science  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
CLASSIFICATION: 9-5 (Biochemical Methods)  
Section cross-reference(s): 1

ABSTRACT:  
Patients with **glycogen storage disease type II** (GSD II) typically excrete increased amts. of a glycogen-derived glucose tetrasaccharide, Glc1-6Glc1-4Glc1-4Glc (Glc4), in the urine. With the advent of a new enzyme replacement therapy for GSD II, there

is a need for early identification of patients with this disease and for monitoring the efficacy of treatment. Glc4 is a good candidate biomarker for GSD II. A simple and robust method using stable isotope dilution-electrospray ionization-**tandem mass spectrometry** for the anal. of Glc4 in biol. samples was developed. A <sup>13</sup>C6-labeled stable isotope internal standard was synthesized by transglycosylation using a recombinant  $\alpha$ -amylase. Bu 4-aminobenzoate derivs. of Glc4 and the internal standard were analyzed using multiple reaction monitoring. This method was shown to be accurate and precise by the repeated anal. of calibrators and quality control samples in urine and plasma. There was good agreement with a high-performance liquid chromatog.-UV method for urine samples, whereas there was less agreement with plasma samples. Accurate determination from dried urine spot samples was also demonstrated. This method is amenable to high-throughput anal., a necessary prerequisite for mass screening for GSD II.

SUPPL. TERM: glucose tetrasaccharide mass spectrometry **glycogen storage disease** urine

INDEX TERM: Blood analysis  
Blood plasma  
HPLC  
Human  
Isotope dilution mass spectrometry  
Quality control  
Urine analysis  
(anal. of a glucose tetrasaccharide elevated in **Pompe** disease by stable isotope dilution-electrospray ionization **tandem mass spectrometry**)

INDEX TERM: **Tandem mass spectrometry**  
(electrospray-ionization; anal. of a glucose tetrasaccharide elevated in **Pompe** disease by stable isotope dilution-electrospray ionization **tandem mass spectrometry**)

INDEX TERM: Electrospray ionization mass spectrometry  
(tandem; anal. of a glucose tetrasaccharide elevated in **Pompe** disease by stable isotope dilution-electrospray ionization **tandem mass spectrometry**)

INDEX TERM: **Glycogen storage disease**  
(type II; anal. of a glucose tetrasaccharide elevated in **Pompe** disease by stable isotope dilution-electrospray ionization **tandem mass spectrometry**)

INDEX TERM: 35175-16-7  
ROLE: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(anal. of a glucose tetrasaccharide elevated in **Pompe** disease by stable isotope dilution-electrospray ionization **tandem mass spectrometry**)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Amalfitano, A; Genet Med 2001, V3, P132 CAPLUS  
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(6) Hallgren, P; J Biol Chem 1977, V252, P1034 CAPLUS  
(7) Kumlien, J; Clin Chim Acta 1988, V176, P39 CAPLUS  
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L2 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:15925 CAPLUS

DOCUMENT NUMBER: 136:131060

ENTRY DATE: Entered STN: 08 Jan 2002

TITLE: Determination of oligosaccharides in **pompe**  
disease by electrospray ionization **tandem**  
**mass spectrometry**

AUTHOR(S): Rozaklis, Tina; Ramsay, Steven L.; Whitfield, Phillip  
D.; Ranieri, Enzo; Hopwood, John J.; Meikle, Peter J.

CORPORATE SOURCE: Lysosomal Diseases Research Unit, Women's and  
Children's Hospital, North Adelaide, South Australia,  
5006, Australia

SOURCE: Clinical Chemistry (Washington, DC, United States)

(2002), 48(1), 131-139

CODEN: CLCHAU; ISSN: 0009-9147

PUBLISHER: American Association for Clinical Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 9-5 (Biochemical Methods)

Section cross-reference(s): 14

ABSTRACT:

Background: The development of therapies for lysosomal storage disorders has created a need for biochem. markers to monitor the efficacy of therapy and methods to quantify these markers in biol. samples. In **Pompe** disease, the concentration of a tetrasaccharide, consisting of four glucose residues, is reputedly increased in urine and plasma, but faster and more sensitive methods are required for the anal. of this, and other oligosaccharides, from biol. fluids. Methods: We optimized the derivatization of storage oligosaccharides with 1-phenyl-3-methyl-5-pyrazolone for the measurement, by electrospray ionization **tandem mass spectrometry**, of oligosaccharide concns. in urine (n = 6), plasma (n = 11), and dried-blood spots (n = 17) from **Pompe**-affected individuals. Age-matched control samples of urine (n = 10), plasma (n = 28), and blood spots (n = 369) were also analyzed. Results: The mean tetrasaccharide concentration was increased in urine from infantile-onset (0.69-12 mmol/ mol. of creatinine) and adult-onset (0.22-3.0 mmol/mol of creatinine) **Pompe** individuals compared with age-matched controls. In plasma samples, an increased tetrasaccharide concentration was observed in some infantile patients (up to 22  $\mu$ mol/L) compared with age-matched controls (mean, 2.2  $\mu$ mol/L). The method developed was sensitive enough to determine oligosaccharide concns. in a single 3-mm blood spot, but no differences were observed between blood spots from control and **Pompe**-affected individuals. Conclusions: Measurements of oligosaccharide concns. in urine by this new method have potential application for the diagnosis and monitoring of patients with **Pompe** disease. Plasma anal. may have limited application for infantile patients, but anal. of blood spots does not discriminate between controls and affected individuals.

SUPPL. TERM: oligosaccharide **pompe** disease electrospray  
ionization **tandem mass**  
**spectrometry**

INDEX TERM: Blood analysis  
Blood plasma  
Body fluid  
Diagnosis  
Human  
**Tandem mass spectrometry**



Urine analysis  
(oligosaccharides determination in **pompe** disease by  
electrospray ionization **tandem mass  
spectrometry**)

INDEX TERM: Oligosaccharides, analysis  
ROLE: ANT (Analyte); THU (Therapeutic use); ANST (Analytical  
study); BIOL (Biological study); USES (Uses)  
(oligosaccharides determination in **pompe** disease by  
electrospray ionization **tandem mass  
spectrometry**)

INDEX TERM: **Glycogen storage disease**  
(type II; oligosaccharides determination in **pompe**  
disease by electrospray ionization **tandem  
mass spectrometry**)

INDEX TERM: 89-25-8, 1-Phenyl-3-methyl-5-pyrazolone  
ROLE: BUU (Biological use, unclassified); BIOL (Biological  
study); USES (Uses)  
(oligosaccharides determination in **pompe** disease by  
electrospray ionization **tandem mass  
spectrometry**)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS  
RECORD.

REFERENCE(S) : (1) An, Y; Anal Biochem 2000, V287, P136 CAPLUS  
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CAPLUS  
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L2 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:904726 CAPLUS

DOCUMENT NUMBER: 136:17717

ENTRY DATE: Entered STN: 14 Dec 2001

TITLE: Diagnostic methods for **Pompe** disease and  
other **glycogen storage  
diseases**

INVENTOR(S) : Millington, David S.; An, Yan; Chen, Yuan Tsong;  
Stevens, Robert D.; Young, Sarah P.; Van Hove, Johan  
L. K.

PATENT ASSIGNEE(S) : Duke University, USA; Van Hove, Johan L. K.

SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
INT. PATENT CLASSIF.:  
MAIN: G01N033-50  
CLASSIFICATION: 9-16 (Biochemical Methods)  
Section cross-reference(s): 14  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094941	A2	20011213	WO 2001-US18288	20010606
WO 2001094941	A3	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002102737	A1	20020801	US 2001-875327	20010606
EP 1360485	A2	20031112	EP 2001-944308	20010606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501365	T2	20040115	JP 2002-502439	20010606
PRIORITY APPLN. INFO.:			US 2000-209920P P	20000607
			WO 2001-US18288 W	20010606

ABSTRACT:

The invention concerns methods of screening subjects for lysosomal storage diseases, preferably **glycogen storage diseases**, using a tetrasaccharide as a biomarker. In a more preferred embodiment, subjects are screened for **Pompe disease** (i.e., **glycogen \*\*\*storage\*\*\* disease type II**). Also provided are neonatal screening assays. The present invention further provides methods of monitoring the clin. condition and efficacy of therapeutic treatment in affected subjects. Further provided are methods of measuring a tetrasaccharide biomarker by **\*\*\*tandem\*\*\* mass spectrometry**, preferably, as part of a neonatal screening assay for **Pompe disease**.

SUPPL. TERM: glycogen storage **Pompe** disease diagnosis  
tetrasaccharide HPLC mass spectrometry

INDEX TERM: Amniotic fluid  
Animal tissue  
Biomarkers (biological responses)  
Blood analysis  
Blood plasma  
Blood serum  
Body fluid  
Cell  
Electrospray ionization mass spectrometry  
**Glycogen storage disease**  
HPLC  
Human  
Immunoassay  
Liquid chromatography  
Lysosomal storage disease  
Mass spectrometry  
Newborn  
Purification  
Sputum  
**Tandem mass spectrometry**  
Urine analysis

(diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: Blood analysis  
(dried blood spot; diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: Standard substances, analytical  
(internal; diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: Ecology  
(population; diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: **Glycogen storage disease**  
(type II; diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: **Glycogen storage disease**  
(type III; diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: **Glycogen storage disease**  
(type VI; diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: 35175-16-7 379261-84-4  
ROLE: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: 89-25-8, 1-Phenyl-3-methyl-5-pyrazolone 93-97-0, Benzoic anhydride 94-25-7, Butyl p-aminobenzoate 27918-14-5, 2-Aminoacridone  
ROLE: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
(diagnostic methods for **Pompe disease and other glycogen storage diseases**)

INDEX TERM: 34620-76-3, Maltopentaose 34620-77-4, Maltohexaose 379261-83-3  
ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)  
(diagnostic methods for **Pompe disease and other glycogen storage diseases**)

L2 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:618188 CAPLUS

DOCUMENT NUMBER: 135:191252

ENTRY DATE: Entered STN: 24 Aug 2001

TITLE: Peptide based DNA sequence identification and analysis and application to detection of polymorphism, mutations, and disease diagnosis

INVENTOR(S): Jarvik, Jonathan W.

PATENT ASSIGNEE(S): Sequel Genetics, Inc., USA

SOURCE: PCT Int. Appl., 63 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:  
MAIN: C12Q

CLASSIFICATION: 3-1 (Biochemical Genetics)  
Section cross-reference(s): 9

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001061028	A2	20010823	WO 2001-US5058	20010216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001041522	A5	20010827	AU 2001-41522	20010216
PRIORITY APPLN. INFO.:			US 2000-182816P	P 20000216
			US 2000-189310P	P 20000314
			WO 2001-US5058	W 20010216

# ABSTRACT:

Rather than examining a DNA mol. by analyzing the DNA itself, in the invention described here the DNA is incorporated into a hybrid artificial gene that is transcribed and translated to produce a hybrid peptide. Phys. anal. of the peptide, in conjunction with informatic anal. of the reference sequence, allows one to identify the sequence of the DNA mol. Specifically, the mass and/or composition and/or partial or complete amino acid sequence of the hybrid peptide is determined, and the data are used to search for matches in data sets produced by in silico transcription and translation of hybrid artificial genes created in silico using the reference sequence, or using transformations of the reference sequence such as

single nucleotide deletions or substitutions thereof. This peptide-based approach to DNA sequence-determination is fundamentally different from all other methods in the art, none of which employs transcription, translation and peptide anal., as does the instant invention. The anal. of peptide reporters provides a number of clear advantages over anal. of the DNA sequences that encode them. One advantage derives from the fact that a peptide is considerably smaller than the DNA that encodes it (individual amino acids avgs. about 110 Da each whereas the trinucleotides (triplets) that encode them average over N Daltons each). Another advantage derives from the fact that peptides are much more diverse in composition than nucleic acids, as they are composed of combinations of 20 different amino acids instead of combinations of 4 different nucleotides. The method can be applied to the identification of genetic mutations and polymorphism, phenotypes, genotyping, disease diagnosis or prognosis. Computer based database, storage medium, and programs for searching and analyzing the data sets, are also claimed. Sequence of the nucleic acid fragments corresponding to the human nucleolin gene and alpha complementing factor of beta-galactosidase gene were correctly identified by the method utilizing MALDI-TOF mass spectrometry anal. of the peptides. Specific genetic mutations and polymorphism were also identified. A computer program for calculating the mass shifts arising from single nucleotide substitutions was developed.

SUPPL. TERM: peptide mass spectrometry analysis DNA sequence detn  
computer program

INDEX TERM: Hemophilia  
(A; peptide based DNA sequence identification and anal.  
and application to detection of polymorphism, mutations,  
and disease diagnosis)

INDEX TERM: Ion cyclotron resonance mass spectrometry  
(Fourier transform, peptide mass determination by; peptide  
based

DNA sequence identification and anal. and application to  
detection of polymorphism, mutations, and disease  
diagnosis)

INDEX TERM: Lipoprotein receptors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological  
study)  
(LDL, deficiency; peptide based DNA sequence

identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Neoplasm  
(Li-Fraumeni syndrome; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Proteins, specific or class  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(MBP (maltose-binding protein), affinity chromatog.; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Phenylketonuria  
(PAX6 Mutation; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Gene, animal  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(RB1, mutation; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Kidney, neoplasm  
(Wilms', Wilm's Tumor; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Immunoglobulins  
(X-linked infantile hypogammaglobulinemia; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Avidins  
Chelates  
Thioredoxins  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(affinity chromatog.; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Purification  
(affinity; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Composition  
(amino acid, phys. property; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Nervous system  
(ataxia telangiectasia; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Liquid chromatography  
(capillary, for peptide purification; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Proteins, specific or class  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(cellulose-binding, affinity chromatog.; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Intestine, neoplasm

(colon, Hereditary non-polypsosis; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Androgen receptors  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
 (deficiency; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Mutation  
 (deletion; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Mutation  
 (duplication; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Escherichia coli  
 (extract, cell free system; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Intestine, neoplasm  
 (familial polyposis; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Capillary electrophoresis  
 Centrifugation  
 Filtration  
 Gel electrophoresis  
 Gel permeation chromatography  
 Liquid chromatography  
 (for peptide purification; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Mitochondria  
 (gene deficiency; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Diagnosis  
 Disease, animal  
 (genetic; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Wheat  
 (germ, extract, cell free system; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Mammary gland  
 Ovary, neoplasm  
 (hereditary breast ovarian cancer syndrome; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Melanoma  
 (hereditary; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Adrenal gland, disease  
 (hyperplasia, Congenital; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Chromatography  
 (immunoaffinity; peptide based DNA sequence identification and anal. and application to detection of

polymorphism, mutations, and disease diagnosis)

INDEX TERM: Immunoassay  
(immunopptn.; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Mutation  
(inversion; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Immunoassay  
(mass spectrometric; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Chromatography  
(membrane, for peptide purification; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Endocrine system  
(neoplasm; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Affinity chromatography  
Alzheimer's disease  
Computer program  
Cystic fibrosis  
DNA sequence analysis  
Databases  
Diabetes mellitus  
Genetic polymorphism  
Genotypes  
Genotyping (method)  
Infection  
Muscular dystrophy  
Mutation  
Neoplasm  
Phenotypes  
Prognosis  
Protein sequence analysis  
Werner syndrome  
(peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Electrospray ionization mass spectrometry  
Mass spectrometry  
**Tandem mass spectrometry**  
Time-of-flight mass spectrometry  
(peptide mass determination by; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Physical properties  
(peptide, assessing; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Laser ionization mass spectrometry  
(photodesorption, matrix-assisted, peptide mass determination by;  
peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Laser desorption mass spectrometry  
(photoionization, matrix-assisted, peptide mass determination by;  
peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and

disease diagnosis)

INDEX TERM: Reticulocyte  
(rabbit extract, cell free system; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Eye, disease  
(retinitis pigmentosa; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Eye, neoplasm  
(retinoblastoma; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Immunodeficiency  
(severe combined, X-linked; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Genetic polymorphism  
(single nucleotide; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Mutation  
(substitution; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Epitopes  
(tag affinity chromatog.; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Recombination, genetic  
(translocation; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Brain, disease  
(tuberous sclerosis; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Collagens, biological studies  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(type I, deficiency; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: **Glycogen storage disease**  
(type II; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Collagens, biological studies  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(type III, deficiency; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: Nervous system  
(von Hippel-Lindau disease; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: 9012-33-3  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(A, deficiency; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

INDEX TERM: 109319-16-6



ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Disease; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)  
 INDEX TERM: 9013-20-1, Streptavidin 50812-37-8, Glutathione S-transferase  
 ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (affinity chromatog.; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)  
 INDEX TERM: 56-73-5, Glucose-6-phosphate 9001-25-6, Blood-coagulation factor VII 9001-29-0, Blood-coagulation factor X 9001-69-8, Ornithine Transcarbamylase 17528-72-2, Tetrahydrobiopterin  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
 (deficiency; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)  
 INDEX TERM: 154210-90-9, GenBank U07148 356612-40-3 356612-41-4 356612-43-6, 17: PN: WO0161051 PAGE: 27 unclaimed DNA 356612-44-7 356612-45-8 356612-46-9 356612-47-0 356612-48-1, 18: PN: WO0161028 PAGE: 29 unclaimed DNA  
 ROLE: PRP (Properties)  
 (unclaimed nucleotide sequence; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)  
 INDEX TERM: 356612-42-5  
 ROLE: PRP (Properties)  
 (unclaimed protein sequence; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)  
 INDEX TERM: 137399-32-7, DNA (human glycoprotein CFTR gene exon 7) 356182-22-4 356182-30-4 356612-37-8 356612-38-9 356612-39-0  
 ROLE: PRP (Properties)  
 (unclaimed sequence; peptide based DNA sequence identification and anal. and application to detection of polymorphism, mutations, and disease diagnosis)

L2 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:804299 CAPLUS  
 DOCUMENT NUMBER: 134:175062  
 ENTRY DATE: Entered STN: 15 Nov 2000  
 TITLE: Liquid chromatographic assay for a glucose tetrasaccharide, a putative biomarker for the diagnosis of **pompe** disease  
 AUTHOR(S): An, Yan; Young, Sarah P.; Hillman, Stephen L.; Van Hove, Johan L. K.; Chen, Yuan-Tsong; Millington, David S.  
 CORPORATE SOURCE: Division of Medical Genetics, Department of Pediatrics, Duke University Medical Center, Research Triangle Park, NC, 27709, USA  
 SOURCE: Analytical Biochemistry (2000), 287(1), 136-143  
 CODEN: ANBCA2; ISSN: 0003-2697  
 PUBLISHER: Academic Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 CLASSIFICATION: 9-3 (Biochemical Methods)  
 Section cross-reference(s): 14  
 ABSTRACT:  
 A HPLC method associated with butyl-p-aminobenzoate derivatization has been

*Applicant*

developed for the anal. of a tetraglucose oligomer, Glc $\alpha$ 1-6Glc $\alpha$ 1-4Glc $\alpha$ 1-4Glc, designated Glc4, in biol. fluids. This tetraglucose, normally excreted in the urine, has previously been shown to be elevated in a number of pathol. conditions including **Pompe disease (glycogen \*\*\*storage\*\*\* disease type II)**, which is caused by a deficiency of the lysosomal enzyme acid  $\alpha$ -glucosidase. Concns. of Glc4 in both urine and plasma were established for the age ranges of <1, 1-5, 6-10, 11-20, and >20 yr, both in normal individuals and in a cohort of 21 patients with enzymically confirmed **Pompe disease**. The Glc4 concentration decreased with age in both groups, but all the patients had elevated Glc4 levels compared with age-matched controls. Electrospray **tandem mass spectrometry** was employed to establish the homogeneity of the HPLC peak for Glc4 and to investigate the identity of other unusual oligosaccharides excreted in patient urine. Our results demonstrate that this method is suitable for application in clin. labs. to help establish the diagnosis of **Pompe disease**. (c)  
2000 Academic Press.

SUPPL. TERM: glucose tetrasaccharide detn HPLC **Pompe disease**  
INDEX TERM: HPLC  
Urine analysis  
(glucose tetrasaccharide detn by HPLC for diagnosis of **Pompe disease**)  
INDEX TERM: **Glycogen storage disease**,  
(type II; glucose tetrasaccharide detn by HPLC for diagnosis of **Pompe disease**)  
INDEX TERM: 35175-16-7  
ROLE: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(tetraglucose; glucose tetrasaccharide detn by HPLC for diagnosis of **Pompe disease**)  
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD.  
REFERENCE(S): (1) Amalfitano, A; Proc Natl Acad Sci 1999, V96, P8861 CAPLUS  
(2) Bijvoet, A; Hum Mol Genet 1999, V8, P2145 CAPLUS  
(3) Brown, B; Biochemistry 1970, V9, P1423 CAPLUS  
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(26) Zopf, D; J Immunol Methods 1982, V48, P109 CAPLUS

ACCESSION NUMBER: 2000:421408 CAPLUS  
 DOCUMENT NUMBER: 133:54508  
 ENTRY DATE: Entered STN: 23 Jun 2000  
 TITLE: Methods and materials for peptide-based DNA sequence determination and analysis  
 INVENTOR(S): Jarvik, Jonathan W.  
 PATENT ASSIGNEE(S): Sequel Genetics, Inc., USA  
 SOURCE: PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
 MAIN: G01N033-48  
 SECONDARY: C12Q001-68; C12P021-06; C12N015-09  
 CLASSIFICATION: 3-1 (Biochemical Genetics)  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000036414	A1	20000622	WO 1999-US30104	19991216
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1151296 A1 20011107 EP 1999-968909 19991216 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO US 2002155445 A1 20021024 US 2001-788268 20010216 PRIORITY APPLN. INFO.: US 1998-112351P P 19981216 WO 1999-US30104 W 19991216 US 2000-182816P P 20000216 US 2000-189310P P 20000314				

ABSTRACT:

A nucleic acid fragment of interest is incorporated into a hybrid artificial gene and expressed in one or more reading frames to produce one or more hybrid polypeptides. The polypeptides are examined with respect to one or more phys. parameters, such as mass or amino acid composition. The observed parameter values are used to search a data set of predicted parameter values generated by hypothetical translation of a larger reference nucleic acid sequence so as to determine whether or not the fragment is contained within the reference sequence, and, if it is contained therein, to determine its sequence and/or coding capacity. The method can be applied to the identification of genetic mutations and polymorphism, phenotypes, genotyping, disease diagnosis or prognosis. Computer based database, storage medium, and programs for searching and analyzing the data sets, are also claimed. Sequence of the nucleic acid fragments corresponding to the human nucleolin gene and alpha complementing factor of beta-galactosidase gene were correctly identified by the method utilizing MALDI-TOF mass spectrometry anal. of the peptides. Specific genetic mutations and polymorphism were also identified. A computer program for calculating the mass shifts arising from single nucleotide substitutions was developed.

SUPPL. TERM: peptide mass spectrometry analysis DNA sequence detn  
 computer program  
 INDEX TERM: Hemophilia  
 (A, diagnosis/prognosis of; methods and materials for  
 peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Muscular dystrophy

(Becker's, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Muscular dystrophy  
(Duchenne, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Ion cyclotron resonance mass spectrometry  
(Fourier transform, for peptide anal.; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Lipoprotein receptors  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(LDL, deficiency, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Neoplasm  
(Li-Fraumeni syndrome, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Time-of-flight mass spectrometry  
(MALDI-, for peptide anal.; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Gene, animal  
ROLE: ANT (Analyte); ANST (Analytical study)  
(PAX6, mutation, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Gene, animal  
ROLE: ANT (Analyte); ANST (Analytical study)  
(RB1, mutation, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Quadrupole mass spectrometry  
(TOF-, for peptide anal.; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Kidney, neoplasm  
(Wilms', hereditary, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Immunoglobulins  
(X-linked infantile hypogammaglobulinemia, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Purification  
(affinity, for peptide purification; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Purification  
(affinity, ligand, for peptide purification; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Nervous system  
(ataxia telangiectasia, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Diagnosis  
(cancer; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Liquid chromatography  
(capillary, for peptide purification; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Intestine, neoplasm  
(colorectal hereditary nonpolyposis carcinoma, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Amino acids, analysis

ROLE: ANT (Analyte); ANST (Analytical study)  
 (composition, anal. of; methods and materials for  
 peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Adrenal cortex, disease  
 (congenital adrenal hyperplasia, diagnosis/prognosis of;  
 methods and materials for peptide-based DNA sequence  
 determination and anal.)  
 INDEX TERM: Centrifugation  
 (deferential, for peptide purification; methods and materials  
 for peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Androgen receptors  
 Mitochondrial DNA  
 ROLE: BSU (Biological study, unclassified); BIOL (Biological  
 study)  
 (deficiency, diagnosis/prognosis of; methods and  
 materials for peptide-based DNA sequence determination and  
 anal.)  
 INDEX TERM: Mutation  
 (deletion; methods and materials for peptide-based DNA  
 sequence determination and anal.)  
 INDEX TERM: Disease, animal  
 (diagnosis of; methods and materials for peptide-based  
 DNA sequence determination and anal.)  
 INDEX TERM: Alzheimer's disease  
 Cystic fibrosis  
 Diabetes mellitus  
 Infection  
 Muscular dystrophy  
 Phenylketonuria  
 Von Willebrand's disease  
 Werner syndrome  
 (diagnosis/prognosis of; methods and materials for  
 peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Mutation  
 (duplication; methods and materials for peptide-based DNA  
 sequence determination and anal.)  
 INDEX TERM: Genetic element  
 ROLE: ANT (Analyte); ANST (Analytical study)  
 (exon, sequence determination; methods and materials for  
 peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Escherichia coli  
 (extract, expression of peptide in; methods and materials  
 for peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Intestine, neoplasm  
 (familial polyposis, diagnosis/prognosis of; methods and  
 materials for peptide-based DNA sequence determination and  
 anal.)  
 INDEX TERM: Electrospray ionization mass spectrometry  
 Mass spectrometry  
**Tandem mass spectrometry**  
 (for peptide anal.; methods and materials for  
 peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Affinity chromatography  
 Capillary electrophoresis  
 Filtration  
 Gel electrophoresis  
 HPLC  
 Liquid chromatography  
 (for peptide purification; methods and materials for  
 peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Computer program  
 (for searching data set; methods and materials for  
 peptide-based DNA sequence determination and anal.)  
 INDEX TERM: Filtration  
 (gel, for peptide purification; methods and materials for

peptide-based DNA sequence determination and anal.)

INDEX TERM: Disease, animal  
(genetic, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Diagnosis  
(genetic; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Wheat  
(germ, extract, expression of peptide in; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Mammary gland  
Mammary gland  
Ovary, neoplasm  
Ovary, neoplasm  
(hereditary breast ovarian cancer syndrome, hereditary, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Melanoma  
(hereditary, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Genotypes  
(heterozygosity, diagnosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Genetic polymorphism  
Phenotypes  
(identification of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Chromatography  
(immunoaffinity, for peptide purification; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Immunoassay  
(immunopptn., mass spectrometric, for peptide purification; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Mutation  
(insertion; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Mutation  
(inversion; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Immunoassay  
(mass spectrometric, for peptide purification; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Peptides, analysis  
ROLE: ANT (Analyte); ANST (Analytical study)  
(mass, composition, or sequence, anal. of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Chromatography  
(membrane, for peptide purification; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: DNA sequence analysis  
Genotyping (method)  
Protein sequence analysis  
Protein sequences  
(methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Endocrine system  
(multiple endocrine neoplasia, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Prognosis  
(of diseases; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Databases  
(of peptide phys. properties; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Reticulocyte  
(rabbit, extract, expression of peptide in; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Eye, disease  
(retinitis pigmentosa, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Eye, neoplasm  
(retinoblastoma, hereditary, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: cDNA  
ROLE: ANT (Analyte); ANST (Analytical study)  
(sequence determination; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Immunodeficiency  
(severe combined, X-linked, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Mutation  
(substitution; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Recombination, genetic  
(translocation; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Brain, disease  
(tuberous sclerosis, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Collagens, biological studies  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(type I, deficiency, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: **Glycogen storage disease**  
(type II, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Collagens, biological studies  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(type III, deficiency, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: Nervous system  
(von Hippel-Lindau disease, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: 9012-33-3  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(A, deficiency, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and anal.)

INDEX TERM: 56-73-5, Glucose-6-phosphate 9001-25-6, Blood-coagulation factor VII 9001-29-0, Factor X 9001-69-8, Ornithine transcarbamylase 17528-72-2, Tetrahydrobiopterin

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(deficiency, diagnosis/prognosis of; methods and materials for peptide-based DNA sequence determination and

anal.)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Darnell, J; Molecular Cell Biology 1986, P109  
(2) Groden; US 5876940 A 1999 CAPLUS  
(3) Housman; US 5702890 A 1997 CAPLUS  
(4) Levine; US 5620848 A 1997 CAPLUS

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
42.04	42.25

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-6.93	-6.93

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